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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 09/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/865,759	SHAPIRO, PHYLLIS	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 6/29/05, are acknowledged. Amended claims 1, 9, 15, 16, and 23 are acknowledged.

Applicant's arguments, filed 6/29/05, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-3 and 5-24 are herein under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5-14, and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

NEW MATTER

Applicant did not point to written support in the specification for the new amendments. The amended limitation "without separation of said red blood cells from said extracellular heme-

colored blood substitute prior to analysis" in claims 1 and 9 does not have written support in the specification, claims, and/or drawings, as originally filed.

Claims 1 (line 5) and 9 (lines 5 and 10) recite "extracellular to said red blood cells" which does not appear to have written support in the specification, claims, and/or drawings, as originally filed. While there is written support for generic "extracellular" limitations, there is no written support for the exogenous heme-colored blood substitute being extracellular specifically to red blood cells.

Therefore, the introduction of these phrases is considered to be NEW MATTER. Claims 2-3, 5-8, 10-14, and 24 are also rejected due to their direct or indirect dependency from instant claims 1 and 9. This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-14, and 24 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These rejections are necessitated by amendment.

Claims 1 (lines 4 and 6), 9 (lines 4 and 6) recite the limitation "said sample. There is insufficient antecedent basis for this limitation in these claims as it is unclear if "said sample" is referring to the previously mentioned "blood sample" or "other sample comprising red blood cells". Clarification of this issue via clearer claim wording is requested. Claims 2-3, 5-8, and

10-14, and 24 are also rejected due to their direct or indirect dependency from instant claims 1 and 9.

Claims 1 and 9 recite "wherein said sample is analyzed on an automated cell-by-cell hematology analyzer" lacks clarity as it is unclear if this limitation is intended to be an active, positive method step or if this "analyzed" limitation is intended to have previously occurred before the method is performed. Clarification of this issue via clearer claim wording is requested. Claims 2-3, 5-8, and 10-14, and 24 are also rejected due to their direct or indirect dependency from instant claims 1 and 9.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chupp et al. (P/N 5,631,165) in view of Chang et al. (P/N 5,200,323), Samsoondar (WO 98/39634), and Rodriguez et al. (P/N 6,228,652).

This rejection is necessitated by amendment.

It is noted that instant claims 1 and 9 recite two sample types: a blood sample or other sample comprising red blood cells. The former sample is anticipated in the prior art.

Chupp et al. teach a system where information about the blood sample is entered into the controller of an automated system that activates the analyzers to perform analyses under the direction of the controller (col. 10, lines 54-67). Chupp et al. describe tests can be performed on the instrument without separating cells from the sample during any phase of the analyses (col. 7, lines 40-46) which represents using a cell hematology analyzer without separating cells from the sample prior to analysis, as stated in instant claims 1 and 9. Chupp et al. describe the system as including an analyzer module, a data station module, and a pneumatic unit (col. 11, lines 27-29). The data station module has "sufficient software algorithms to manipulate measured data, calculate parameters and display results in a variety of formats" (col. 11, lines 62-67). Chupp et al. further discuss the analyzer module in which sample tubes of blood are automatically transported with bar code labels that can be read with a bar code reader so that sample information can be inputted into the system controller (col. 25, lines 22-35) as stated on lines 2-3 of instant claims 1, 12-13, and 19-20. Chupp et al. teach correcting MCH and MCHC in blood (as stated in instant claims 1, 9, and 21-23) by performing the mathematical computations described in (a) through (d) of instant claim 1 and b(1) – (2) of instant claim 9 where the constants to correct dimension units for formula 1 is 10 and for formula 2 is 100 (col. 53, lines 66-67 and col. 54, lines 1-26), as stated in instant claims 14 and 24. Chupp et al. teach the use of setting hemoglobin flags if any results are abnormal or suspect (col. 61, lines 50-51) which suggests the blood sample tested may be normal or abnormal as stated in claim 3. Chupp et al. also describe anemic patients with increased reticulocyte counts as indicating rapid erythroid turnover suggesting acute blood loss or hemolysis (col. 1, lines 62-65) as stated in claims 5 and 6. However, Chupp et al. do not teach the presence of an extracellular hemoglobin product or

oxygen-carrying blood substitute such as recombinant human hemoglobin, isolation and purification from animal blood, cell-by-cell measurements, or subtraction of the blood substitute correction factor from the original reported chemistry result.

Chang et al. describe hemoglobin which carries oxygen to tissues (col. 2, lines 40-43) and the use of modified hemoglobin blood substitutes as alternatives to human donor blood, such as recombinant human hemoglobin (col. 3, lines 61-63) which is an extracellular hemoglobin product or oxygen-carrying blood substitute, as stated in instant claims 2, 7, 10, and 17. Chang et al. describe adding modified hemoglobin blood substitutes to a human plasma sample with a centrifugation step (abstract) which represents isolation and purification of animal blood (as stated in instant claims 8, 11, and 18) as well as being extracellular to red blood cells (which are absent), as stated in instant claims 1 and 9. Chang et al. do not describe cell-by-cell measurements or the subtraction of the blood substitute correction factor from the original reported chemistry result.

Samsoondar describes a method of identifying and quantifying the concentration of a blood substitute (abstract). Samsoondar describes a method of taking the measured concentration of the blood substitute and correcting for its effect on a measured analyte concentration, such as serum/plasma total protein (abstract). Samsoondar describes making the necessary adjustment or correction to the measured analyte concentration to remove the effect of the blood substitute (page 5, lines 5-9) which represents a subtraction of the blood substitute correction factor from the original reported chemistry result, as stated in instant claims 16 and 23. Figure 3 (with the linear calibration mathematical formula) provides results of a linear regression fit of data generated from true Hb calibration (fitted Hb value) in the presence of

cross-linked hemoglobin (blood substitute) and other interferents (actual Hb value) (page 5, lines 20-22) which represents a correction factor multiplied by the hemoglobin value scaled to the appropriate units of dimensions of the reported analytes to correct for interference, as stated in instant claim 16 and 23. Samsoondar describes quantifying the relationship between measured amounts of each analyte with respect to the blood substitute present in the serum or plasma specimen (page 18, lines 23-26). In an example, Samsoondar describes finding the actual serum total hemoglobin concentration by subtracting the blood substitute times the slope of the regression line (correction factor) from the measured value (page 23, lines 4-15). Samsoondar describes determining the concentration of true hemoglobin in the presence of blood substitutes (abstract). Samsoondar describes using samples contained in labeled tubes in a blood analyzer (abstract). Samsoondar describes a user can specify a particular interferent to be analyzed (page 11, lines 2-4). Samsoondar describes screening samples by taking successive sample measurements for interferents and blood substitutes (page 11, second paragraph).

Rodriguez et al. describe a blood analyzing instrument (abstract) and taking measurements on every cell where measurement data are processed to yield a report of cells and cellular hemoglobin information including mean volumes for a sample (col. 13, lines 20-33). Rodriguez et al. describe measuring cell-by-cell hemoglobin (col. 13, lines 34-42), as stated in instant claims 1, 9, and 15.

Chupp et al. describe the presence of classes and subclasses of red blood cells (col. 3, lines 53-54) and how the two methods used can distinguish cells and subdivide the cell types into finer classifications (col. 3, lines 7-14). Chupp et al. also discuss the need for increasing the precision and accuracy of previous manual methods of hematology analysis by using automated

systems (col. 7, lines 11-16). Chang et al. point out it would be highly desirable to screen human blood and plasma to determine the safety of modified hemoglobin blood substitutes for humans (col. 4, lines 11-30). Samsoondar states that although cross-linked hemoglobin blood substitutes data are collected in his invention, it is understood that similar calibration algorithms for measuring other blood substitutes and correcting for their effects on blood test results, are within the scope of his invention (page 12, lines 12-16). For the reasons set forth above, one of ordinary skill in the art would have been motivated to use the automated hematology analyzer and method for correcting MCH and MCHC values in blood, as stated by Chupp et al., for all types of blood samples in use at the time of the invention such as those containing modified hemoglobin blood substitutes, as stated by Chang et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use samples including recombinant human hemoglobin and other modified hemoglobin blood substitutes (as stated by Chang et al. and Samsoondar) in automated methods and systems of obtaining accurate MCH and MCHC values (as stated by Chupp et al. and Samsoondar) including the successive cell-by-cell measurements as exemplified by Rodriquez et al., because this information would enhance understanding of safety and potential problems of the various types of blood and blood substitutes in humans at the time of the invention, as stated by Chang et al. (col. 4, lines 11-30). Thus, Chupp et al., in view of Chang et al., Samsoondar, and Rodriguez et al., motivate the limitations in claims 1-3 and 5-24 of the instant invention.

Applicant summarizes the invention. Applicant states she has amended claims 1, 9, 15, and 16 to point out the invention measures intracellular and total hemoglobin without prior

separation of the sample to its cellular and plasma components. It is noted that it is unclear if the added "analyze" limitation involving separation is an active method step.

Applicant summarizes the Chupp et al. reference. Applicant states there is no teaching of blood substitutes and other various limitions. This statement is found unpersuasive as these limitations are taught in the other references in the 35 USC 103 rejection.

Applicant summarizes the Chang et al. reference. Applicant states Chang et al. add the blood substitute to human plasma, which lacks cellular hemoglobin. It is noted that Chang et al. was relied upon for the use of recombinant human hemoglobin limitations as well as isolation and purification from animal blood. Applicant argues that Chang et al. do not disclose measuring methods or correcting hematology values. This statement is unpersuasive as these limitations are addressed in the other references.

Applicant summarizes the Rodriquez reference. Applicant argues that Rodriquez does not measure the level of a blood substitute or correct hematology values. This statement is unpersuasive as these limitations are addressed in the other references.

Applicant summarizes the Samsoondar reference. Applicant argues that Samsoondar does not do cell-by-cell measurements. This statement is unpersuasive as this limitation is addressed in the Rodriquez et al. reference.

Applicant argues that none of the cited references teach or suggest intracellular hemoglobin. It is noted that the way the claims are written with two possible samples, one sample does not contain the intracellular hemoglobin, and it was this sample which is addressed in the prior art rejection of record. It is noted that intact red blood cells would be expected to inherently comprise hemoglobin, therefore lysed (or otherwise damaged) red blood cells would

be expected to release hemoglobin. A sample comprising lysed red blood cells (i.e. Chupp et al., col. 12, lines 1-9) would therefore necessarily comprise intracellular hemoglobin.

Applicant argues that there is no suggestion to make the suggested modification. This statement is found unpersuasive as increasing precision and accuracy of hematology analysis by using automated systems is taught by Chupp et al. and the desirability of screening blood and plasma for safety with modified hemoglobin blood substitutes is taught by Chang et al. Additional motivation was stated as the information would enhance understanding safety and potential problems of the various blood types and blood substitutes (as stated by Chang et al.).

Applicant argues that Chupp et al. is silent with respect to extracellular blood substitutes. This statement is found unpersuasive as a single reference does not need to contain all of the recited limitations, which is why the claims are rejected under 35 USC 103 and not a 35 USC 102. Applicant argues that Chang et al. do not suggest the problem solved by the present invention. This statement is found unpersuasive as the motivation to combine references need not be the same as those of the instant invention. Applicants argue that Rodriquez et al.'s measurement of erythrocyte by cell-by-cell hemoglobin and Samsoondar's removal of red cells would be inoperative. It is noted that various aspects of the claims are taken from the prior art references as a whole. One of ordinary skill in the art reasonably would have expected success to combine these references, because the prior art references all deal with analyzing blood samples. Applicant mentions the "without prior separation" step that has been amended in the claims. It is noted that it is unclear if this lack of prior separation step is actually an active step in instant claims 1 and 9 or not. Applicant argues that paragraph 42 contains a clear and concise definition of "cellular hemoglobin". It is noted that paragraph 42 does not set forth any

definition. Applicant argues Chupp et al. do not distinguish cellular from extracellular hemoglobin and the term "hemoglobin" used by Chupp et al. is clearly not the "cellular hemoglobin" or intracellular hemoglobin of the instant invention. It is noted that intact red blood cells would be expected to inherently comprise hemoglobin, therefore lysed (or otherwise damaged) red blood cells would be expected to release hemoglobin. A sample comprising lysed red blood cells (i.e. Chupp et al., col. 12, lines 1-9) would therefore necessarily comprise intracellular hemoglobin. Applicant's arguments are deemed unpersuasive.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
9/8/05

September 6, 2005